Appendix 1: Prevention and assessment of Tuberculosis (TB) in refugees and migrants

Rationale

In 2013, there were estimated to be over 340,000 new or relapsed cases of tuberculosis in Europe. There has been a steady decline in overall TB incidence rates in most European countries over the past four decades. This decrease has been more marked in the local-born population whereas cases among the foreign born have decreased more slowly or in some countries have actually risen during this time period.[1] This health disparity is primarily due to migration of individuals from intermediate and high TB burden countries. Migrants from these countries are at increased risk of exposure to TB, leading to asymptomatic latent TB that has the potential to reactivate into cases of active and transmissible TB.

Screening and treatment of active and latent TB are important components of TB control strategies. Individuals with TB are usually symptomatic, potentially infectious and may be detected through chest radiography screening. Persons with latent TB are asymptomatic, non-infectious and are detected with a tuberculin skin test or an interferon gamma release assay blood test (IGRA). The yield of chest radiograph screening to detect active TB in asymptomatic populations is relatively low and does not detect those with latent TB. Tests for latent TB have different operational characteristics however they are limited by the fact that the timing of infection cannot be determined and the minority of those with positive tests will reactivate in the future unless they are very young, have been recently infected (<2 years) or have certain concomitant medical co-morbidities. Therefore, the majority of asymptomatic patients with LTBI take therapy that may not be necessary and that may be associated with adverse reactions including hepatotoxicity that requires close monitoring.

Objectives

1. To determine if migrants from TB endemic countries arriving or living in Europe should be screened for active TB. And if yes, who should be targeted and how?
2. To determine if migrants from TB endemic countries arriving or living in Europe should be screened for latent TB? And if yes, who should be targeted and how?

<u>What is the yield and cost-effectiveness of screening migrants for active TB?</u>

Key questions

1. What is the yield of CXR screening in migrants and how does this vary with the TB incidence in migrant source countries, by migrant class, by age?
2. In what setting does CXR have the highest yield of detecting active TB? Pre-entry, upon arrival or post arrival to low TB incidence countries?
3. What are the test performance characteristics of CXR to detect active TB?
4. How effective is active TB therapy and what are the associated harms?
5. How cost-effective is screening for active TB in migrants. Are there particular sub-groups or settings in which it is more cost-effective?
6. How does cost-effectiveness change with TB incidence in TB source countries?
7. What is the acceptability (uptake) of active TB screening programs by migrants?

Population Important Outcomes:

1. Prevalence of active TB
2. TB hospitalizations (due to delayed detection)
3. TB mortality (due to delayed detection)
4. TB transmission to others
5. Quality of life due to development of active TB

6. Yield of active TB on CXR overall and by TB incidence in source countries; setting (pre, upon, and post landing)
7. Effectiveness and harms of active TB Treatment
8. Cost-effectiveness and resource use of active TB screening programs

<u>Does routine latent TB screening and providing latent TB therapy in migrants decrease active TB incidence in low incidence countries?</u>

Key Questions

1. What is the baseline risk of developing active TB in immigrants and how does this differ by source country of origin, immigration class?
2. What is the relative risk of developing active TB in the presence of underlying medical co-morbidities?
3. What tests should be used for screening? TST, IGRA or sequential TST/IGRA
4. What are the test properties?
5. What LTBI therapy should be given? 9INH, 6INH, 4Rif, 3INH/Rifapentine, 3RH.
   a) What is the effectiveness of LTBI therapy to prevent active TB?
   b) What are the side effect profiles (harms) of the different LTBI therapies?
6. What is the acceptance and knowledge of the need for screening and providing LTBI therapy by health care providers?
7. What is the acceptance/knowledge of the need for screening and taking LTBI therapy in the migrant population?
8. What proportion of patients complete LTBI treatment?
9. What characterizes the change in resource use and costs involved in effective TB screening strategies? What is the incidence threshold in migrant source countries for which LTBI screening is cost-effective? (In Canada, screen if 30/100,000; in the UK, screen if 150/100,000)

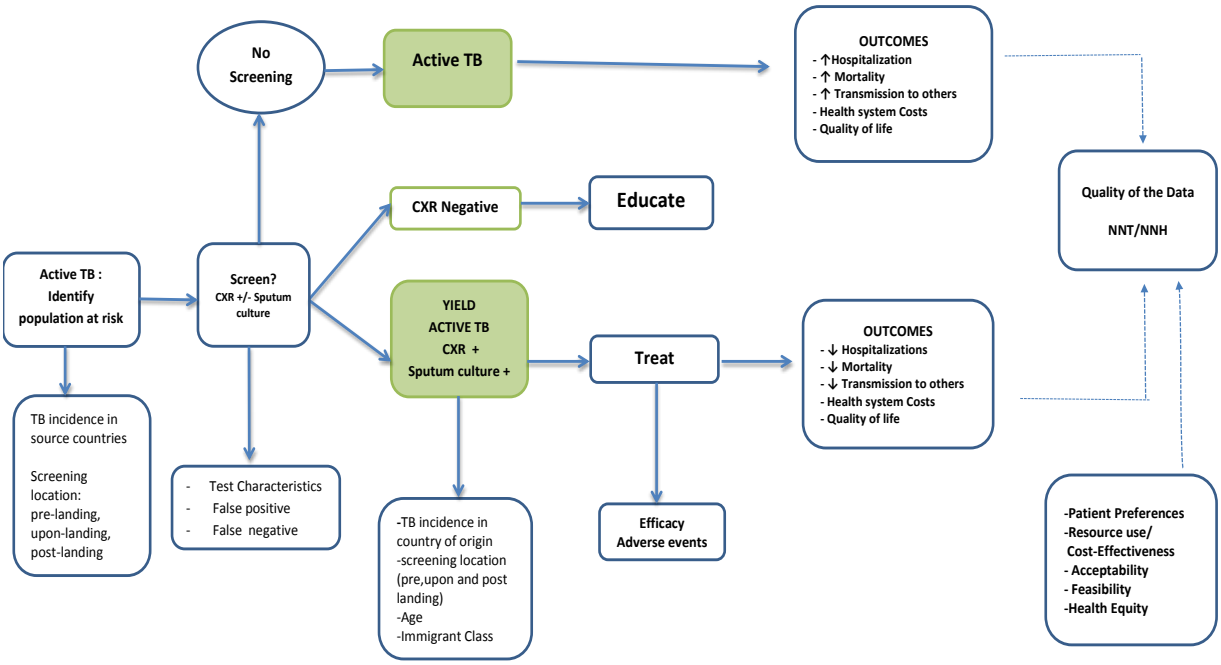
Population important outcomes:

1. Incidence of active TB
2. Active TB hospitalizations (due to reactivation)
3. TB mortality (due to delayed detection)
4. TB transmission to others
5. Quality of life due to active TB treatment regimens, and remissions (no active disease), development of active TB
6. Test accuracy measures (TST, IGRA, sequential TST, IGRA): sensitivity, specificity, likelihood ratios, predictive values
7. Effectiveness and serious adverse events of due to each LTBI treatment regimen
8. Resource use, costs and cost-effectiveness of latent TB screening/treatment programs

References

1. European Centre for Disease Prevention and Control. Guidance on tuberculosis control in vulnerable and hard-to-reach populations. 2016. http://ecdc.europa.eu/en/publications/_layouts/forms/Publication_DispForm.aspx?List=4f55ad51-4aed-4d32-b960-af70113dbb90&ID=1451 (accessed September 2016)

Appendix 1 - Figure 1: Logic model, Active Tuberculosis



Appendix 1 - Figure 2: Logic model, Latent Tuberculosis